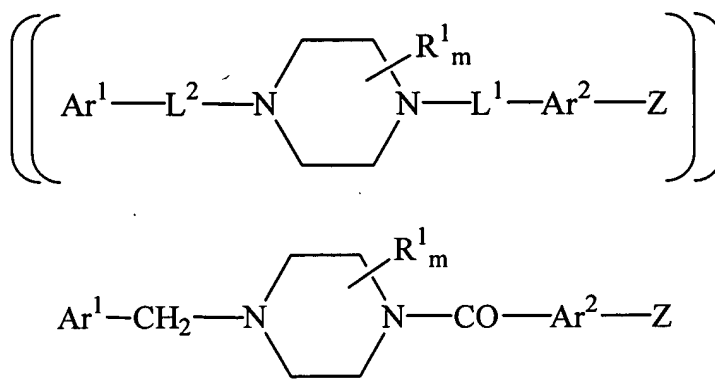


**CLAIM AMENDMENTS**

1. (currently amended): A compound of the formula:



or the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein:

$\text{Ar}^1$  is an aryl group substituted with 0-5 non-interfering substituents, ~~wherein two adjacent noninterfering substituents can form a fused aromatic or nonaromatic ring selected from the group~~ consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR,  $\text{NR}_2$ , SR, SOR,  $\text{SO}_2\text{R}$ , OCOR, NRCOR,  $\text{NRCONR}_2$ ,  $\text{NRCOOR}$ ,  $\text{OCONR}_2$ , RCO, COOR, alkyl-OOCR,  $\text{SO}_3\text{R}$ ,  $\text{CONR}_2$ ,  $\text{SO}_2\text{NR}_2$ ,  $\text{NRSO}_2\text{NR}_2$ , CN,  $\text{CF}_3$ ,  $\text{R}_3\text{Si}$ , and  $\text{NO}_2$ , wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl or heteroaryl, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members;

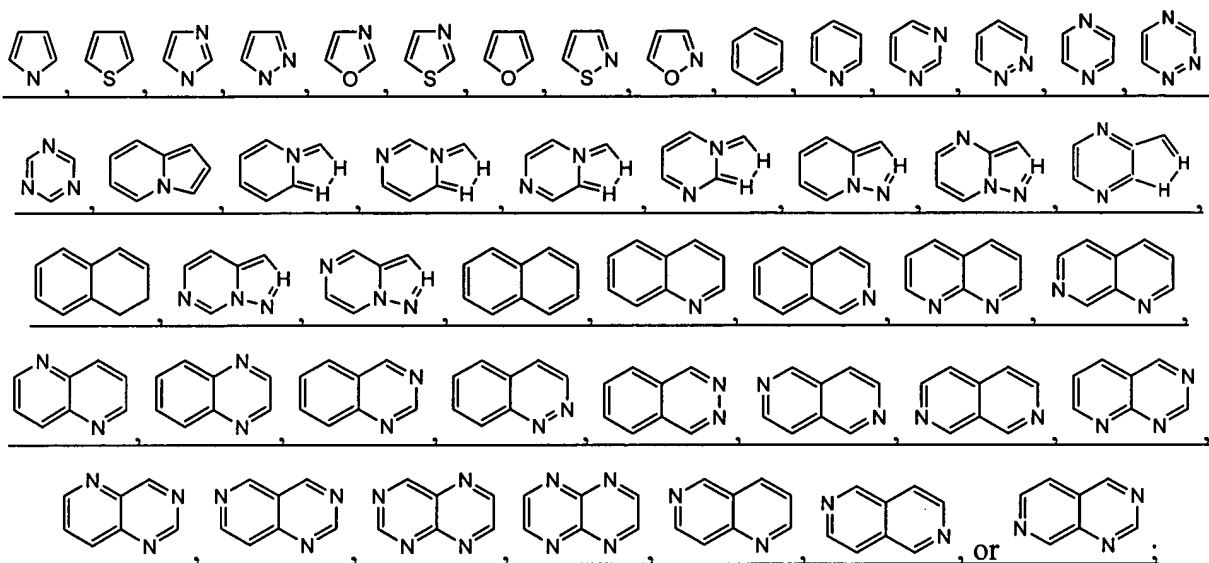
$\text{L}^1$  and  $\text{L}^2$  are linkers;

each  $\text{R}^1$  is independently a noninterfering substituent selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR,  $\text{NR}_2$ , SR, SOR,  $\text{SO}_2\text{R}$ , OCOR, NRCOR,  $\text{NRCONR}_2$ ,  $\text{NRCOOR}$ ,  $\text{OCONR}_2$ , RCO, COOR, alkyl-OOCR,  $\text{SO}_3\text{R}$ ,  $\text{CONR}_2$ ,  $\text{SO}_2\text{NR}_2$ ,  $\text{NRSO}_2\text{NR}_2$ , CN,  $\text{CF}_3$ ,  $\text{R}_3\text{Si}$ , and  $\text{NO}_2$ , wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl or heteroaryl and two of  $\text{R}^1$  on adjacent positions can be joined to form a

fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R<sup>1</sup> is =O or an oxime, oximeether, oximeester or ketal thereof;

m is 0-4;

Ar<sup>2</sup> is a substantially planar, monocyclic or polycyclic aromatic moiety having one or more optional ring heteroatoms, said moiety being optionally substituted with one or more non-interfering substituents, two or more of which may form a fused ring phenyl,



wherein H is N or CR'

wherein R' is hydrogen or

(a) alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl or halo; or

(b) OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOCR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, R<sub>3</sub>Si, and NO<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl or heteroaryl;

and wherein two R' can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members;

Z is -W<sub>i</sub>-COX<sub>j</sub>Y wherein Y is COR<sup>3</sup> or an isostere thereof tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole; R<sup>3</sup> is [[a]] H or a noninterfering substituent which is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, SOR, SO<sub>2</sub>R, SO<sub>2</sub>NR<sub>2</sub>, OR, NR<sub>2</sub>,

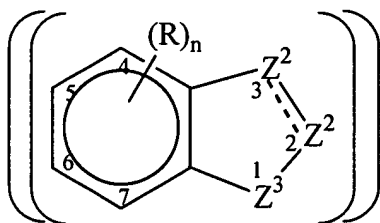
OCOR, NRCOR, NRCONR<sub>2</sub>, NRSO<sub>2</sub>R, NRSO<sub>2</sub>NR<sub>2</sub>, OCONR<sub>2</sub>, CN, COOR, CONR<sub>2</sub>, COR, or R<sub>3</sub>Si  
wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl or heteroaryl, or


wherein R<sup>3</sup> is OR, NR<sub>2</sub>, SR, NRCONR<sub>2</sub>, OCONR<sub>2</sub>, or NRSO<sub>2</sub>NR<sub>2</sub>, wherein each R is  
independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl or heteroaryl, and

wherein two R attached to the same atom may form a 3-8 member carbocyclic or  
heterocyclic ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl,  
arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR,  
NR<sub>2</sub>, OCOR, NRCOR, NRCONR<sub>2</sub>, NRSO<sub>2</sub>R, NRSO<sub>2</sub>NR<sub>2</sub>, OCONR<sub>2</sub>, or R<sub>3</sub>Si wherein each R is  
independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl or heteroaryl wherein two R  
attached to the same atom may form a 3-8 member ring, optionally substituted as above defined,

~~each of W and X is a spacer an alkylene of 2-6 Å, and each of i and j is independently 0 or 1;~~  
~~wherein the distance in space between the atom of Ar<sup>1</sup> bonded to L<sup>2</sup> and the atom of Ar<sup>2</sup>~~  
~~bonded to L<sup>1</sup> is no more than 24 angstroms;~~

~~with the proviso that the portion of the compound represented by Ar<sup>2</sup>-Z is not~~



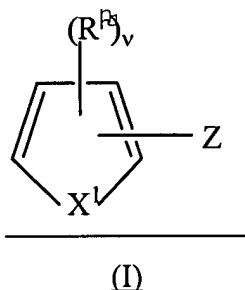
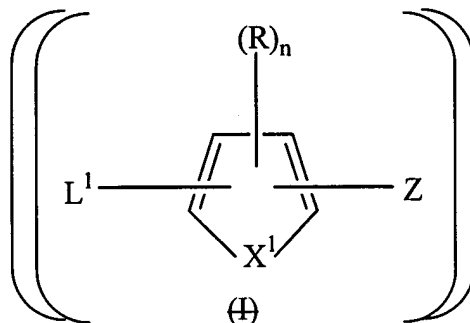
~~wherein  represents a single or double bond; n is 0-3; one Z<sup>2</sup> is CA or CRA and the~~  
~~other is CR, CR<sub>2</sub>, NR or N; A is -W, -COX, Y wherein Y is COR or an isostere thereof, each of W~~  
~~and X is a spacer of 2-6 Å, and each of i and j is independently 0 or 1; Z<sup>3</sup> is NR or O; and each R is~~  
~~independently hydrogen or a noninterfering substituent.~~

2-5. (canceled)

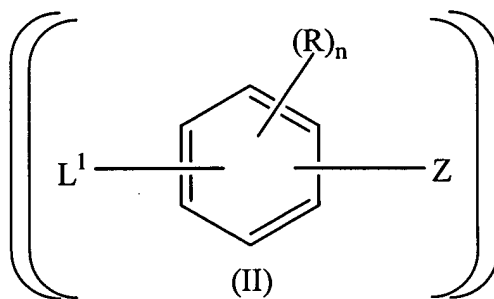
6. (original): The compound of claim 1 wherein each of i and j is 0.

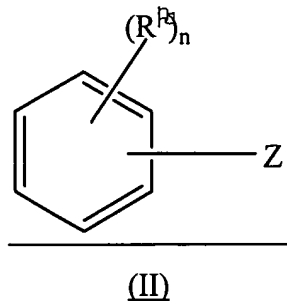
7-9. (canceled)

10. (currently amended): The compound of ~~claim 8~~ claim 1 wherein the portion of said compound represented by  $[[L^1-Ar^2-Z]]$   $Ar^2-Z$  is selected from the following:

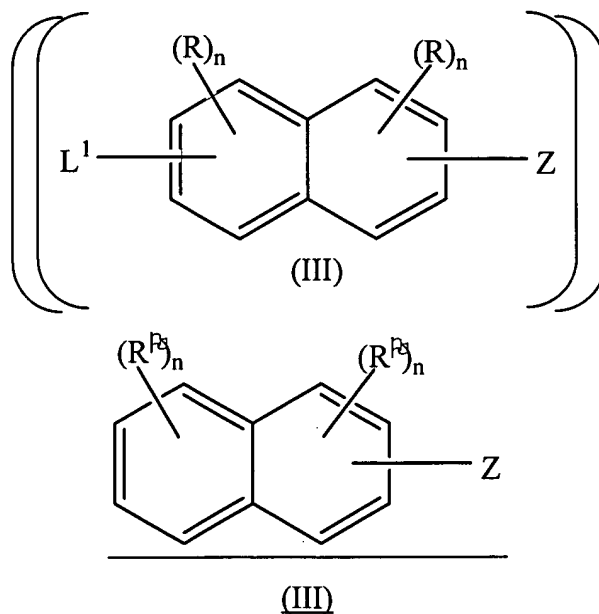


wherein  $n$  is 0, 1 or 2;  $X^1$  is  $NR$ ,  $CR_2$ ,  $O$  or  $S$ ,  $NR''$  or  $CR''_2$ ; and each  $[[R]]$   $R''$  is O independently ~~H or a noninterfering substituent~~ selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR,  $NR_2$ , SR, NRCOR, alkyl-OOCR, RCO, COOR, and CN, wherein each  $R$  is independently H, alkyl, aryl, heteroalkyl, or heteroaryl; and two or more  $[[R]]$   $R''$  groups may form a fused ring;

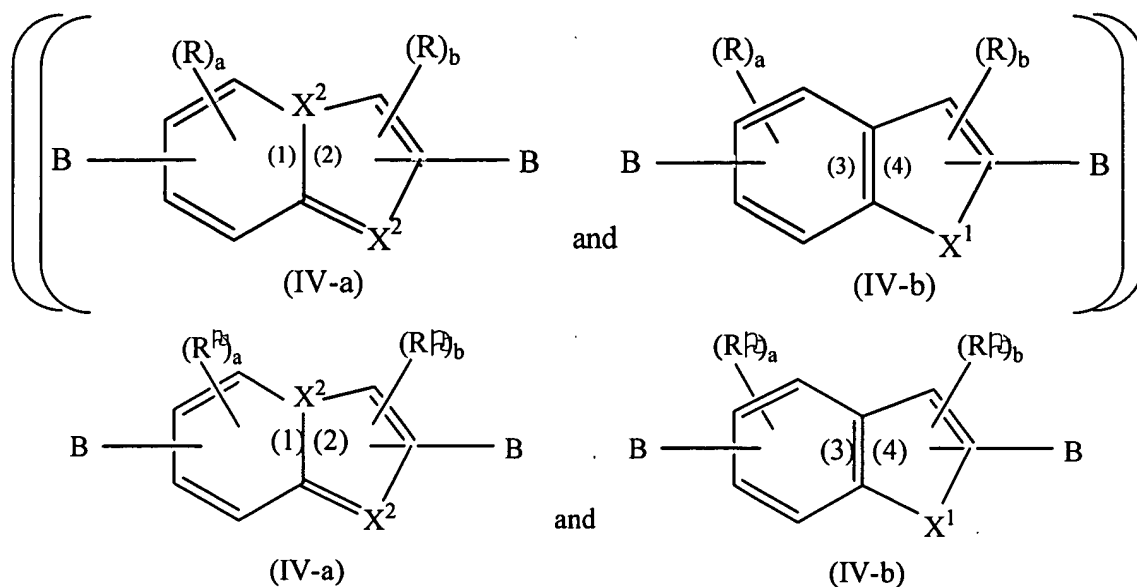




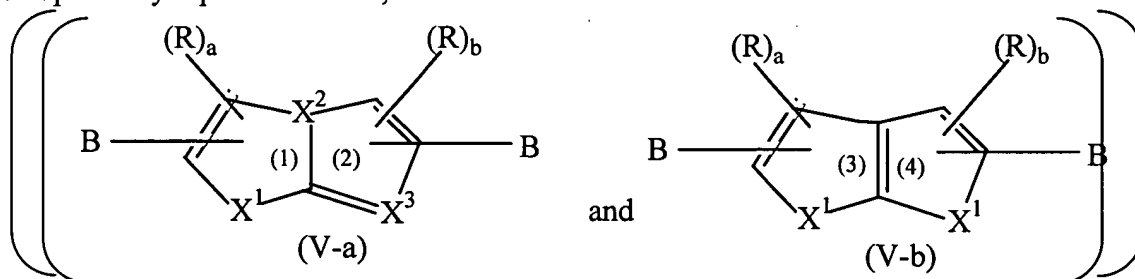
wherein n is 0-4; ~~R is H or a noninterfering substituent~~ R is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR<sub>2</sub>, SR, NRCOR, alkyl-OOCR, RCO, COOR, and CN, wherein each R is independently H, alkyl, aryl, heteroalkyl, or heteroaryl where two or more ~~[[R]]~~ RO groups may form a fused ring; and one or more ring carbons may be optionally replaced with nitrogen;

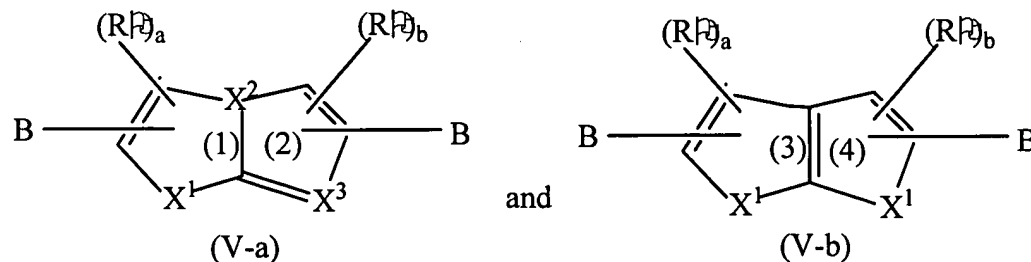


wherein each n is independently 0 to 3; ~~R is H or a noninterfering substituent~~ R is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR<sub>2</sub>, SR, NRCOR, alkyl-OOCR, RCO, COOR, and CN, wherein each R is independently H, alkyl, aryl, heteroalkyl, or heteroaryl, where two or more ~~[[R]]~~ RO groups may form a fused ring; and one or more ring carbons may be optionally replaced with nitrogen;



wherein, ~~subject to the proviso of claim 1, one B is  $[[L^1]]$  absent and the other is Z; wherein a is 0 to 4 [such that the positions on the six membered rings (1) and (3) to which (R) is bonded can include  $X^2$  when  $X^2$  is C]; b is 0-3 [such that the positions on the five membered rings (2) and (4) to which (R)b is bonded can include  $X^2$  and  $X^1$ , when  $X^2$  is C and  $X^1$  is N or C] each  $X^2$  is independently N or  $[[CR]]$  CRO;  $X^1$  is NR,  $CR_2$ , O or S NRO or CRO<sub>2</sub>; each  $[[R]]$  RO is H or a noninterfering substituent independently selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR<sub>2</sub>, SR, NRCOR, alkyl-OOCR, RCO, COOR, and CN, wherein each R is independently H, alkyl, aryl, heteroalkyl, or heteroaryl where two or more  $[[R]]$  RO groups may form a fused ring; wherein one or more of the ring carbons that are at positions other than  $X^2$  or  $X^1$  and that are also not bound to B or to the remainder of the molecule can be optionally replaced with N;~~

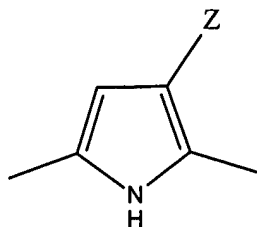




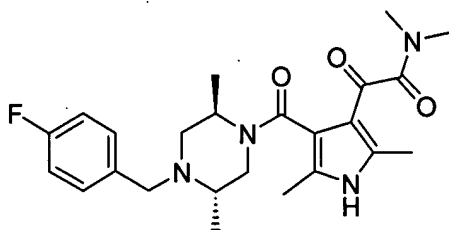
wherein one B is ~~[[L<sup>+</sup>]] absent~~ and the other is Z; a is 0-4 ~~[[such that the positions on the rings (1) and (3) to which (R)<sub>a</sub> can be bonded include X<sup>2</sup> and X<sup>1</sup>], [[where X<sup>2</sup> is C and X<sup>1</sup> is C or N]]~~; b is 0-3 ~~[[such that the positions on the rings (2) and (4) to which (R)<sub>b</sub> can be bonded include X<sup>1</sup>, X<sup>2</sup> and X<sup>3</sup> when X<sup>1</sup> is C or N and X<sup>2</sup> and/or X<sup>3</sup> are C]]~~; each X<sup>1</sup> is independently ~~[[NR, CR<sub>2</sub>, O or S]]~~ NRO or CRO<sub>2</sub>; X<sup>2</sup> and X<sup>3</sup> are independently N or CR; ~~each R CRO; each RO is~~ independently H or a noninterfering substituent selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR<sub>2</sub>, SR, NRCOR, alkyl-OOCR, RCO, COOR, and CN, wherein each R is independently H, alkyl, aryl, heteroalkyl or heteroaryl where two or more R groups can optionally form a fused ring; wherein one or more of the ring carbons that are at positions other than X<sup>1</sup>, X<sup>2</sup> or X<sup>3</sup>, and that are also not bound to B or to the remainder of the molecule, can be optionally replaced with N.

11-15. (canceled)

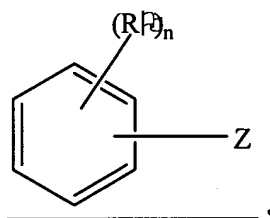
16. (currently amended): The compound of ~~claim 15~~ claim 10 wherein ~~structure (I)~~ Ar<sup>2</sup>-Z is:



17. (previously presented): The compound of claim 16 where the compound is:



18. (currently amended): The compound of claim 10 wherein  $[[L^1-Ar^2-Z]]$   $Ar^2-Z$  is structure (II):



19. (currently amended): The compound of claim 18 wherein ~~the R in structure (II)~~ each RO is methoxy.

20. (currently amended): The compound of claim 19 wherein ~~n in structure (II)~~ is 1.

21-22. (canceled)

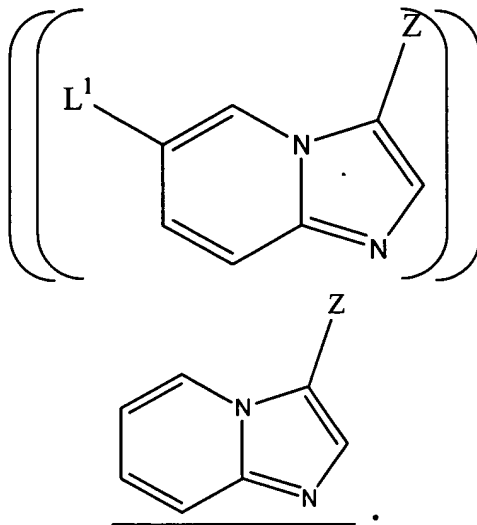
23. (currently amended): The compound of claim 10 wherein  $[[L^1-Ar^2-Z]]$   $Ar^2-Z$  is structure (III).

24. (currently amended): The compound of claim 10 wherein  $[[L^1-Ar^2-Z]]$   $Ar^2-Z$  is structure (IV-a) or (IV-b).

25. (currently amended): The compound of claim 24 wherein  $[[L^1-Ar^2-Z]]$   $Ar^2-Z$  is (IV-a) and both  $X^2$  in structure (IV-a) are nitrogen.



26. (currently amended): The compound of claim 25 wherein ~~structure (IV)~~ Ar<sup>2</sup>-Z is:



27. (canceled)

28. (currently amended): The compound of ~~claim 8~~ claim 10 wherein ~~[[L<sup>1</sup>-Ar<sup>2</sup>-Z]]~~ Ar<sup>2</sup>-Z is structure (V-a) or (V-b).

29. (currently amended): The compound of claim 28 wherein ~~[[L<sup>1</sup>-Ar<sup>2</sup>-Z]]~~ Ar<sup>2</sup>-Z is structure (V-a) and X<sup>2</sup> and X<sup>3</sup> in structure (V-a) are N.

30. (currently amended): The compound of claim 29 wherein at least one ~~[[R]]~~ RO in structure ~~[[V]]~~ (V-a) is methyl.

- 31-42. (canceled)

43. (currently amended): The compound of ~~claim 42~~ claim 1 wherein Ar<sup>1</sup> is optionally substituted phenyl.

44. (original): The compound of claim 43 wherein said optional substitution is by halo, OR, or alkyl.

45. (original): The compound of claim 44 wherein said phenyl is unsubstituted or has a single substituent.

46. (canceled)

47. (currently amended): The compound of ~~claim 46~~ claim 1 wherein each R<sup>1</sup> is halo, OR, or alkyl.

48. (original): The compound of claim 47 wherein m is 0, 1, or 2.

49. (original): The compound of claim 48 wherein m is 2 and both R<sup>1</sup> are alkyl.

50-52. (canceled)

53. (previously presented): A pharmaceutical composition for treating conditions characterized by enhanced p38- $\alpha$  activity which composition comprises a therapeutically effective amount of a compound of claim 1 along with a pharmaceutically acceptable excipient.

54-56. (canceled)

57. (currently amended): A method to treat a condition mediated by p38- $\alpha$  kinase comprising administering to a subject in need of such treatment a compound of claim 1 or a pharmaceutical composition thereof, wherein said condition is multiple sclerosis, IBD, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, sepsis, endotoxic shock, asthma, adult respiratory distress syndrome, reperfusion injury, psoriasis, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, a bone resorption disease, graft-versus-host reaction, Crohn's Disease, ulcerative colitis, or pyresis.

58-60. (canceled)